

CLAIMS

1. Use of polypeptides corresponding to the envelope proteins of PTLV, or fragments or
5 sequences derived thereof, said polypeptides being selected for their ability to bind
specifically to the ubiquitous vertebrate glucose transporter GLUT1 represented by SEQ ID
NO : 2, or of nucleotide sequences encoding said polypeptides, for the preparation of drugs
for the prevention or the treatment of pathologies linked to an overexpression of GLUT1 on
cell surfaces, and the *in vitro* diagnosis of said pathologies.

10 2. Use according to claim 1, of polypeptides able to bind to at least one of the following
fragments of GLUT1 :

- SEQ ID NO : 25 : NAPQKVIEEFY
- SEQ ID NO : 26 : NQTWVHRYGESILPTTLTTLWS
- 15 - SEQ ID NO : 27 : KSFEMILGR
- SEQ ID NO : 28 : DSIMGNKDL
- SEQ ID NO : 29 : YSTSIFEKAGVQQP
- SEQ ID NO : 30 : EQLPWMSYLS
- SEQ ID NO : 31 : QYVEQLC
- 20 - SEQ ID NO : 32 : IVGMC FQYVEQLC

3. Use according to claim 1 or 2, of polypeptides able to bind to at least the following
fragment of GLUT1 :

- SEQ ID NO : 32 : IVGMC FQYVEQLC

25 4. Use according to any of claims 1 to 3, of GLUT1 binding polypeptides chosen among
the followings :

- the envelope protein of HTLV-1 corresponding to SEQ ID NO : 4, or of HTLV-2
corresponding to SEQ ID NO : 6, or of STLV-1 corresponding to SEQ ID NO : 8, or of
30 STLV-2 corresponding to SEQ ID NO : 10, or of STLV-3 corresponding to SEQ ID NO : 12,
- fragments of the envelope proteins of PTLV, said fragments corresponding to
polypeptides delimited in their N-terminal extremity by the amino acid located in position 1 to
90, or in position 75 to 90, and in their C-terminal extremity by the amino acid located in

position 135 to 245, or in position 135 to 150, of said envelope proteins of PTLV, such as SEQ ID NO : 4, 6, 8, 10, 12,

- fragments of the envelope proteins of PTLV, said fragments corresponding to the following polypeptides :

5 * the polypeptide delimited in its N-terminal extremity by the amino acid located in position 83 to 89, and in its C-terminal extremity by the amino acid located in position 139 to 145, of the envelope protein of the strain MT-2 of HTLV-1 corresponding to SEQ ID NO : 4,

 * the polypeptide delimited in its N-terminal extremity by the amino acid located in position 79 to 85, and in its C-terminal extremity by the amino acid located in position 135 to 141, of the envelope protein of the strain NRA of HTLV-2 corresponding to SEQ ID NO : 6,

 * the polypeptide delimited in its N-terminal extremity by the amino acid located in position 83 to 89, and in its C-terminal extremity by the amino acid located in position 139 to 145, of the envelope protein of STLTV-1 corresponding to SEQ ID NO : 8,

 * the polypeptide delimited in its N-terminal extremity by the amino acid located in position 79 to 85, and in its C-terminal extremity by the amino acid located in position 135 to 141, of the envelope protein of STLTV-2 corresponding to SEQ ID NO : 10,

 * the polypeptide delimited in its N-terminal extremity by the amino acid located in position 82 to 88, and in its C-terminal extremity by the amino acid located in position 138 to 144, of the envelope protein of STLTV-3 corresponding to SEQ ID NO : 12,

20 * the polypeptide corresponding to the envelope protein of a variant of HTLV-1, said polypeptide having the following sequence SEQ ID NO : 14,

I	K	K	P	N	P	N	G	G	G	Y	Y	L	A	S	Y	S	D
P	C	S	L	K	C	P	Y	L	G	C	Q	S	W	T	C	P	Y
T	G	A	V	S	S	P	Y	W	K	F	Q	Q	D	V			

25 * the polypeptide corresponding to the envelope protein of a variant of HTLV-1, said polypeptide having the following sequence SEQ ID NO : 16,

V	K	K	P	N	R	N	G	G	G	Y	Y	L	A	S	Y	S	D
P	C	S	L	K	C	P	Y	L	G	C	Q	S	W	T	C	P	Y
T	G	A	V	S	S	P	Y	W	K	F	Q	Q	D	V			

30 * the polypeptide corresponding to the envelope protein of a variant of HTLV-1, said polypeptide having the following sequence SEQ ID NO : 18,

I	K	K	P	N	R	N	G	G	G	Y	Y	L	A	S	Y	S	D
P	C	S	L	K	C	P	Y	L	G	C	Q	S	W	T	C	P	Y
T	G	A	V	S	S	P	Y	W	K	F	Q	Q	D	V			

* the polypeptide corresponding to the envelope protein of a variant of HTLV-1, said polypeptide having the following sequence SEQ ID NO : 20,

I K K P N R N G G G Y Y L A S Y S D
P C S L K C P Y L G C Q S W T C P Y
5 T G P V S S P Y W K F Q Q D V

* the polypeptide corresponding to the envelope protein of a variant of HTLV-1, said polypeptide having the following sequence SEQ ID NO : 22,

I K K P N R N G G G Y H S A S Y S D
C S L K C P Y L G C Q S W T C P Y A
10 A V S S P Y W K F Q Q D V N F T Q E

* the polypeptide corresponding to the envelope protein of a variant of HTLV-2, said polypeptide having the following sequence SEQ ID NO : 24,

I R K P N R Q G L G Y Y S P S Y N D
P C S L Q C P Y L G S Q S W T C P Y
15 T A P V S T P S W N F H S D V

5. Use of GLUT1 binding polypeptides according to any of claims 1 to 4, characterized in that the pathologies are the followings :

- solid tumors, such as brain tumors, squamous cell carcinoma, hypopharyngeal
20 carcinoma, breast cancer, cervical carcinoma, ovarian carcinoma, pancreatic cancer, insulinoma,

- inflammatory conditions, such as multiple sclerosis, rheumatoid arthritis,
- immune or auto-immune diseases, such as autoimmune myocarditis, or in the frame of
CD28 T-cell activation, or in the frame of immunomodulation, or systemic lupus
25 erythematosus,

- disorders of the central nervous system, such as facilitated glucose transporter protein type 1 (GLUT1) deficiency syndrome.

6. Use according to any of claims 1 to 5, of GLUT1 binding polypeptides for the *in vitro*
30 detection of GLUT1 on cell surfaces in the frame of processes for the *in vitro* diagnosis of pathologies linked to an overexpression of GLUT1 on cell surfaces, such as pathologies defined in claim 5, said processes comprising the following steps :

- contacting a biological sample from an individual with a GLUT1 binding polypeptide, said GLUT1 binding polypeptide being optionally labeled, or susceptible to be recognized by
35 a labeled molecule,

- determining the level of said GLUT1 binding polypeptide bound to the cells contained in the biological sample and comparison with the level of binding of said GLUT1 binding polypeptide to cells contained in the biological sample from an healthy individual.

5 7. Use according to any of claims 1 to 5, of GLUT1 binding polypeptides, or of nucleotide sequences encoding said polypeptides, for the preparation of drug vectors containing at their surface said polypeptides, said vectors being useful for targeting GLUT1 overexpressing cells for the prevention or the treatment of pathologies linked to an overexpression of GLUT1 on cell surfaces, said vectors containing molecules active against
10. said pathologies, or containing genes in the frame of gene therapy of these pathologies.

8. Use according to claim 7, for the preparation of drug vectors containing at their surface GLUT1 binding polypeptides, said vectors being useful for targeting GLUT1 overexpressing tumor cells, or cells involved in the inflammatory mechanism, or activated
15. cells of the immune system, or cells of the central nervous system, for the prevention or the treatment of pathologies defined in claim 5.

9. Use according to claim 7 or 8, wherein the molecules active against the pathologies are antitumor molecules, or molecules against inflammatory conditions, immune or auto-
20. immune diseases, or disorders of the central nervous system.

10. Therapeutic vectors useful for targeting GLUT1 overexpressing cells in pathologies linked to an overexpression of GLUT1 on cell surfaces, such as pathologies defined in claim 5, said vectors containing at their surface GLUT1 binding polypeptides chosen among those
25. defined in claims 1 to 4, and containing molecules active against said pathologies, as defined in claim 9, or containing genes in the frame of gene therapy.

11. Pharmaceutical compositions containing therapeutic vectors according to claim 10, in association with a pharmaceutically acceptable carrier.

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12. Method for the screening of compounds useful for the prevention or the treatment of pathologies linked to an overexpression of GLUT1 on cell surfaces, and the *in vitro* diagnosis of said pathologies, comprising :

- the contacting of GLUT1 represented by SEQ ID NO : 2, or of fragments as defined in claim 2, or sequences derived thereof, said fragments or derived sequences being able to bind to the envelope proteins of the primate T-cell leukemia viruses (PTLV), or of cells expressing GLUT1, with compounds to be tested,

- 5 - the selection of compounds able to bind specifically to GLUT1, or fragments or sequences derived thereof.

13. Method for the *in vitro* diagnosis of pathologies linked to an overexpression of GLUT1 on cell surfaces, characterized in that it comprises :

- 10 - contacting a biological sample from an individual with polypeptides selected for their ability to bind specifically to GLUT1 as defined in claims 1 to 4, said polypeptides being optionally labeled, or susceptible to be recognized by a labeled molecule,
- determining the level of said polypeptides bound to the cells contained in the biological sample and comparison with the level of binding of said polypeptides to cells
- 15 contained in the biological sample from an healthy individual.

14. Method according to claim 13 for the *in vitro* diagnosis of pathologies defined in claim 5.

- 20 15. Kit for the *in vitro* diagnosis of pathologies linked to an overexpression of GLUT1 on cell surfaces according to the method of claim 13 or 14, comprising GLUT1 binding polypeptides as defined in claims 1 to 4, said polypeptides being optionally labeled, and, if necessary reagents for the detection of the binding of said polypeptides to GLUT1 initially present on cell surfaces in the biological sample.

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